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=> s fgl2
L2 54 FGL2

=> dup remove l2
PROCESSING COMPLETED FOR **L2**
L3 29 DUP REMOVE L2 (25 DUPLICATES REMOVED)

=> d l3 1-29 ti au so ab ibib

L3 ANSWER 1 OF 29 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
TI Genomic characterization, localization, and functional expression of **FGL2**, the human gene encoding fibroleukin: A novel human procoagulant.
AU Yuwaraj S.; Ding J.W.; Liu M.; Marsden P.A.; Levy G.A.
SO Genomics, (1 Feb 2001) 71/3 (330-338).
Refs: 67
ISSN: 0888-7543 CODEN: GNMCEP
AB For diseases in which thrombosis plays a pivotal role, such as virus-induced fulminant hepatitis, fetal loss syndrome, and xenograft rejection, the major procoagulant has remained elusive. Here we describe the isolation and functional expression of a distinct human prothrombinase, termed **FGL2**. The routine **fgl2** gene product has been implicated in tile pathophysiology of routine fulminant hepatitis. The predicted ORF corresponds to a 439-amino-acid type II integral membrane protein that contains a carboxy-terminal Fibrinogen-related domain. Functional analysis showed that **FGL2** -encoded protein is indeed a prothrombinase. This enzyme is a serine protease and directly cleaves prothrombin to thrombin. The **FGL2** gene is a single-copy gene in the haploid human genome and has two exons separated by a 2195-bp intron expressing two mRNA transcripts of 1.5 and 5.0 kb. Tile 5'-flanking region contains putative cis-elements including a TATA box, an AP1 site, CEBP sites, Spl site, and Ets binding domains. By both radiation hybrid analyses and fluorescence in situ hybridization, human **FGL2** was localized to 7q11.23. .COPYRGT. 2001 Academic Press.
ACCESSION NUMBER: 2001080181 EMBASE
TITLE: Genomic characterization, localization, and functional expression of **FGL2**, the human gene encoding fibroleukin: A novel human procoagulant.
AUTHOR: Yuwaraj S.; Ding J.W.; Liu M.; Marsden P.A.; Levy G.A.
CORPORATE SOURCE: G.A. Levy, Multiorgan Transplant Program, Toronto General Hospital, 621 University Avenue, Toronto, Ont. M5G 2C4, Canada. fgl2@msn.com

SOURCE: Genomics, (1 Feb 2001) 71/3 (330-338).
Refs: 67
ISSN: 0888-7543 CODEN: GNMCEP
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 2 OF 29 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 2
TI **Fgl2** prothrombinase expression in mouse trophoblast and decidua triggers abortion but may be countered by OX-2.
AU Clark D.A.; Ding J.-W.; Yu G.; Levy G.A.; Gorczynski R.M.
SO Molecular Human Reproduction, (2001) 7/2 (185-194).
Refs: 49
ISSN: 1360-9947 CODEN: MHREFD
AB Spontaneous abortion of normal karyotype embryos in mice and in humans is associated with an increase in uterine T helper (Th) 1 type proinflammatory cytokines, tumour necrosis factor (TNF)-.alpha., interferon-.gamma. and interleukin (IL)-1, and a deficiency of Th2/3 type cytokines, IL-4, IL-10, and transforming growth factor (TGF)-.beta.2. In mice, Th1 cytokines up-regulate a novel prothrombinase, **fgl2**, which via thrombin, leads to activation of polymorphonuclear leukocytes that terminate the pregnancy. Here we show that Th1 cytokines up-regulate **fgl2** mRNA in fetal trophoblast and secondary decidua of CBA/J x DBA/2 and CBA/J x BALB/c matings, and promote fibrin deposition. This pattern is accompanied by a high rate of abortion. However, the spontaneous abortion rates in abortion-prone CBA x DBA/2 matings and in low abortion rate CBA x BALB/c matings were significantly lower than that expected from the frequency of implantations with high levels of fibrin and **fgl2** mRNA(hi). As the glycoprotein OX-2 occurs in the pregnant rat uterus and can deviate cytokine responses to Th2/3, we investigated OX-2 in pregnant CBA/J mice. We found OX-2 mRNA was present at the same sites as **fgl2** mRNA, but was reduced in response to Th1 cytokines. Furthermore, anti-OX-2 raised the abortion rate to predicted levels, while recombinant OX-2 dramatically reduced the abortion rate. **Fgl2** prothrombinase may provide a mechanism explaining pregnancy loss, and conversely, successful pregnancy may be due in part to OX-2-dependent activation of maternal tolerance mechanisms at the feto-maternal interface.
ACCESSION NUMBER: 2001064410 EMBASE
TITLE: **Fgl2** prothrombinase expression in mouse trophoblast and decidua triggers abortion but may be countered by OX-2.
AUTHOR: Clark D.A.; Ding J.-W.; Yu G.; Levy G.A.; Gorczynski R.M.
CORPORATE SOURCE: D.A. Clark, Dept. of Med., Pathol./Molec. Med., Dept. of Obstetrics and Gynecology, McMaster University, 1200 Main St West, Hamilton, Ont. L8N 3Z5, Canada. clarkd@fhs.McMaster.ca
SOURCE: Molecular Human Reproduction, (2001) 7/2 (185-194).
Refs: 49
ISSN: 1360-9947 CODEN: MHREFD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 010 Obstetrics and Gynecology
025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2001 ACS
TI Modulators of **fgl2** prothrombinase for inhibiting virus-induced immune coagulation
IN Levy, Gary
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
AB The inventor has detd. that the nucleocapsid protein from a hepatitis virus can induce the prothrombinase fgl-2. The inventor has further developed that LF-A1 also induces fgl-2. This allows for the development of therapeutic methods and compns. for modulating immune coagulation. In particular, inhibitors of the N-protein or gene or LF-A1 protein gene, or LF-A1 binding site on the fgl-2 promoter may be useful in inhibiting immune coagulation caused by a virus such as a hepatitis virus.
ACCESSION NUMBER: 2000:628020 CAPLUS
DOCUMENT NUMBER: 133:227716
TITLE: Modulators of **fgl2** prothrombinase for inhibiting virus-induced immune coagulation
INVENTOR(S): Levy, Gary
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051636	A1	20000908	WO 2000-CA191	20000225

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-122109 19990226
REFERENCE COUNT: 11
REFERENCE(S):
(1) Ding, J; Biennial Scientific Meeting of the International Association for the Study of the Liver and the 49th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases 1998
(6) Mizutani, T; JOURNAL OF VETERINARY MEDICAL SCIENCE 1994, V56(2), P211 CAPLUS
(9) Ning, Q; JOURNAL OF BIOLOGICAL CHEMISTRY 1999, V274(15), P9930 CAPLUS
(10) Stohlman, S; VIROLOGY 1994, V202(1), P146 CAPLUS

(11) Zhong, W; US 5849485 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
TI Immune coagulation in preeclampsia.
AU Knackstedt, M.; Johnson, N. (1); Yu, K. (1); Ding, J. W. (1); Levy, G. A. (1); Gorczynski, R. (1); Clark, D. A. (1)
SO FASEB Journal, (April 20, 2000) Vol. 14, No. 6, pp. A1248. print.
Meeting Info.: Joint Annual Meeting of the American Association of Immunologists and the Clinical Immunology Society Seattle, Washington, USA
May 12-16, 2000
ISSN: 0892-6638.
ACCESSION NUMBER: 2001:40038 BIOSIS
DOCUMENT NUMBER: PREV200100040038
TITLE: Immune coagulation in preeclampsia.
AUTHOR(S): Knackstedt, M.; Johnson, N. (1); Yu, K. (1); Ding, J. W. (1); Levy, G. A. (1); Gorczynski, R. (1); Clark, D. A. (1)
CORPORATE SOURCE: (1) MRC Group on Organ Injury, Toronto Hospital, Univ. of Toronto, Toronto, ON Canada
SOURCE: FASEB Journal, (April 20, 2000) Vol. 14, No. 6, pp. A1248. print.
Meeting Info.: Joint Annual Meeting of the American Association of Immunologists and the Clinical Immunology Society Seattle, Washington, USA May 12-16, 2000
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 5 OF 29 MEDLINE DUPLICATE 3
TI Molecular and functional analysis of the human prothrombinase gene (HFGL2)
and its role in viral hepatitis.
AU Levy G A; Liu M; Ding J; Yuwaraj S; Leibowitz J; Marsden P A; Ning Q; Kovalinka A; Phillips M J
SO AMERICAN JOURNAL OF PATHOLOGY, (2000 Apr) 156 (4) 1217-25.
Journal code: 3RS. ISSN: 0002-9440.
AB In the present studies, we report the cloning and structural characterization of the HFGL2 gene and its functional role in human fulminant hepatitis. The HFGL2 gene is approximately 7 kb in length with 2
exons. The putative promoter contains cis element consensus sequences that
strongly suggest the inducibility of its expression. From the nucleotide sequence of the human gene, a 439-amino acid long protein is predicted. The overall identity between the murine **fgl2** and hfgl2 coded proteins is over 70%. About 225 amino acids at the carboxyl end of these molecules are almost 90% identical, and correspond to a well-conserved fibrinogen-related domain. Both HFGL2 and **FGL2** encode a type II transmembrane protein with a predicted catalytic domain toward the amino terminus of the protein. Transient transfection of Chinese hamster ovary (CHO) cells with a full-length cDNA of HFGL2 coding region resulted in high levels of prothrombinase activity. Livers from 8 patients transplanted for fulminant viral hepatitis were examined for extent of necrosis, inflammation, fibrin deposition, and HFGL2 induction. In situ hybridization showed positive staining of macrophages in areas of active hepatocellular necrosis. Fibrin stained positively in these areas and was

confirmed by electron microscopy. These studies define a unique prothrombinase gene (HFGL2) and implicate its importance in the pathogenesis of fulminant viral hepatitis.

ACCESSION NUMBER: 2000216630 MEDLINE
DOCUMENT NUMBER: 20216630
TITLE: Molecular and functional analysis of the human prothrombinase gene (HFGL2) and its role in viral hepatitis.
AUTHOR: Levy G A; Liu M; Ding J; Yuwaraj S; Leibowitz J; Marsden P A; Ning Q; Kovalinka A; Phillips M J
CORPORATE SOURCE: Multi Organ Transplant Program, Toronto General Hospital and The University of Toronto, Toronto, Ontario, Canada.. fgl2@msn.com
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (2000 Apr) 156 (4) 1217-25. Journal code: 3RS. ISSN: 0002-9440.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 200009
ENTRY WEEK: 20000901

L3 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2001 ACS
TI The transcriptional signature of dioxin in human hepatoma HepG2 cells
AU Puga, A.; Maier, A.; Medvedovic, M.
SO Biochem. Pharmacol. (2000), 60(8), 1129-1142
CODEN: BCPCA6; ISSN: 0006-2952
AB The authors have used a high d. microarray hybridization approach to characterize the transcriptional response of human hepatoma HepG2 cells to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The authors find that exposure to 10 nM TCDD for 8 h alters by at least a factor of 2.1 the expression of 310 known genes and of an equiv. no. of expressed sequence tags. Treatment with TCDD in the presence of 20 .mu.g/mL of cycloheximide blocked the effect on 202 of these genes, allowing us to distinguish between primary effects of TCDD exposure, which take place whether cycloheximide is present or not, and secondary effects, which are blocked by inhibition of protein synthesis. Of the 310 known genes affected by TCDD, 30 are up-regulated and 78 are down-regulated regardless of cycloheximide treatment, and 84 are up-regulated and 118 are down-regulated only when protein synthesis is not inhibited. Functional clustering of genes regulated by TCDD reveals many potential physiol. interactions that might shed light on the multiple biol. effects of this compd. These results, however, suggest that arriving at a sound understanding of the mol. mechanisms governing the biol. outcome of TCDD exposure promises to be orders of magnitude more complicated than might have been previously imagined.

ACCESSION NUMBER: 2000:677037 CAPLUS
DOCUMENT NUMBER: 134:52467
TITLE: The transcriptional signature of dioxin in human hepatoma HepG2 cells
AUTHOR(S): Puga, A.; Maier, A.; Medvedovic, M.
CORPORATE SOURCE: Center for Environmental Genetics and Department of Environmental Health, University of Cincinnati Medical Center, Cincinnati, OH, 45267-0056, USA

SOURCE: Biochem. Pharmacol. (2000), 60(8), 1129-1142
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 188
REFERENCE(S): (1) Abbott, B; Toxicology 1995, V105, P365 CAPLUS
(3) Ballou, L; Biochim Biophys Acta 1996, V1301, P273 CAPLUS
(5) Bertazzi, P; Sci Total Environ 1991, V106, P5 CAPLUS
(6) Bingham, C; Proc Assoc Am Physicians 1999, V111, P516 CAPLUS
(8) Bjerke, D; Toxicol Appl Pharmacol 1994, V127, P241
CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
TI Domain I of nucleocapsid protein of MHV-3 induces transcription of **fgl2** prothrombinase gene and accounts for fulminant viral hepatitis.
xenoserum?
AU Levy, Gary A. (1); Ning, Qin (1); Liu, Mingfeng (1); Lakatoo, Sophie (1); Phillips, Melville James (1); Lai, Michael Mmc.; Fung, Laisum
SO Hepatology, (October, 2000) Vol. 32, No. 4 Pt. 2, pp. 381A. print.
Meeting Info.: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000 American Association for the Study of Liver Diseases
. ISSN: 0270-9139.
ACCESSION NUMBER: 2000:506334 BIOSIS
DOCUMENT NUMBER: PREV200000506334
TITLE: Domain I of nucleocapsid protein of MHV-3 induces transcription of **fgl2** prothrombinase gene and accounts for fulminant viral hepatitis.
AUTHOR(S): Levy, Gary A. (1); Ning, Qin (1); Liu, Mingfeng (1); Lakatoo, Sophie (1); Phillips, Melville James (1); Lai, Michael Mmc.; Fung, Laisum
CORPORATE SOURCE: (1) Toronto Gen Hosp, Toronto, ON Canada
SOURCE: Hepatology, (October, 2000) Vol. 32, No. 4 Pt. 2, pp. 381A.
print.
Meeting Info.: 51st Annual Meeting and Postgraduate Courses
of the American Association for the Study of Liver Diseases
Dallas, Texas, USA October 27-31, 2000 American Association
for the Study of Liver Diseases
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 8 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
TI Targeted disruption of the **fgl2** gene prevents fulminant hepatitis.
AU Levy, Gary A. (1); Fung, Laisum (1); Phillips, Melville J. (1); Marsden, Philip A. (1)

SO Hepatology, (October, 2000) Vol. 32, No. 4 Pt. 2, pp. 381A. print.
Meeting Info.: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000 American Association for the Study of Liver Diseases . ISSN: 0270-9139.

ACCESSION NUMBER: 2000:506333 BIOSIS
DOCUMENT NUMBER: PREV200000506333
TITLE: Targeted disruption of the **fgl2** gene prevents fulminant hepatitis.
AUTHOR(S): Levy, Gary A. (1); Fung, Laisum (1); Phillips, Melville J. (1); Marsden, Philip A. (1)
CORPORATE SOURCE: (1) Toronto Gen Hosp, Toronto, ON Canada
SOURCE: Hepatology, (October, 2000) Vol. 32, No. 4 Pt. 2, pp. 381A.
print.
Meeting Info.: 51st Annual Meeting and Postgraduate Courses
of the American Association for the Study of Liver Diseases
Dallas, Texas, USA October 27-31, 2000 American Association
for the Study of Liver Diseases
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 9 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
TI The liver specific cis-element HNF4 is essential for transcription of **fgl2** prothrombinase gene in response to nucleocapsid protein of MHV-3 and responsible for mouse fulminant viral hepatitis.
AU Levy, Gary A. (1); Ning, Qin (1); Liu, Mingfeng (1); Lakatoo, Sophie (1); Phillips, Melville James (1); Lai, Michael Mmc.; Fung, Laisum
SO Hepatology, (October, 2000) Vol. 32, No. 4 Pt. 2, pp. 380A. print.
Meeting Info.: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA October 27-31, 2000 American Association for the Study of Liver Diseases . ISSN: 0270-9139.

ACCESSION NUMBER: 2000:503773 BIOSIS
DOCUMENT NUMBER: PREV200000503773
TITLE: The liver specific cis-element HNF4 is essential for transcription of **fgl2** prothrombinase gene in response to nucleocapsid protein of MHV-3 and responsible for mouse fulminant viral hepatitis.
AUTHOR(S): Levy, Gary A. (1); Ning, Qin (1); Liu, Mingfeng (1); Lakatoo, Sophie (1); Phillips, Melville James (1); Lai, Michael Mmc.; Fung, Laisum
CORPORATE SOURCE: (1) Toronto Gen Hosp, Toronto, ON Canada
SOURCE: Hepatology, (October, 2000) Vol. 32, No. 4 Pt. 2, pp. 380A.
print.
Meeting Info.: 51st Annual Meeting and Postgraduate Courses
of the American Association for the Study of Liver Diseases
Dallas, Texas, USA October 27-31, 2000 American Association
for the Study of Liver Diseases

. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 10 OF 29 MEDLINE DUPLICATE 4
TI The nucleocapsid protein of murine hepatitis virus type 3 induces transcription of the novel **fgl2** prothrombinase gene.
AU Ning Q; Liu M; Kongkham P; Lai M M; Marsden P A; Tseng J; Pereira B; Belyavskyi M; Leibowitz J; Phillips M J; Levy G
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Apr 9) 274 (15) 9930-6.
Journal code: HIV. ISSN: 0021-9258.
AB Using a set of parental and recombinant murine hepatitis virus strains, we
demonstrate that the nucleocapsid protein induces transcription of the novel **fgl2** prothrombinase gene and elevated procoagulant activity in those strains that produce fulminant hepatitis. Chinese hamster ovary cells cotransfected with a construct expressing nucleocapsid
protein from susceptible strains and with a luciferase reporter construct containing the **fgl2** promoter showed a 6-fold increase in luciferase activity compared with nontransfected cells or cells cotransfected with a construct expressing nucleocapsid protein from resistant strains. Two deletions found at coding sites 111-123 and 1143-1145 of structural domains I and III, respectively, of the nucleocapsid gene may account for the differences between pathogenic and nonpathogenic strains. Preliminary mapping of the **fgl2** promoter has defined a region from -372 to -306 upstream from the ATG translation initiation site to be responsive to nucleocapsid protein. Hence, mapping of genetic determinants in parental and recombinant strains demonstrates that the nucleocapsid protein of strains that induce fulminant hepatitis is responsible for transcription of the **fgl2** prothrombinase gene. These studies provide new insights into the role of the nucleocapsid
gene in the pathogenesis of viral hepatitis.
ACCESSION NUMBER: 1999214542 MEDLINE
DOCUMENT NUMBER: 99214542
TITLE: The nucleocapsid protein of murine hepatitis virus type 3 induces transcription of the novel **fgl2** prothrombinase gene.
AUTHOR: Ning Q; Liu M; Kongkham P; Lai M M; Marsden P A; Tseng J; Pereira B; Belyavskyi M; Leibowitz J; Phillips M J; Levy G
CORPORATE SOURCE: Multi-Organ Transplant Program and Departments of Medicine and Pathology, Toronto Hospital, St. Michael's Hospital, and the University of Toronto, Toronto, Ontario M5G 2C4, Canada.
CONTRACT NUMBER: AI30169 (NIAID)
AI19244 (NIAID)
NS18146 (NINDS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Apr 9) 274 (15) 9930-6.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-AF025817
ENTRY MONTH: 199907

ENTRY WEEK: 19990702

L3 ANSWER 11 OF 29 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Erratum: Cutting edge: Cytokine-dependent abortion in CBA x DBA/2 mice is mediated by the procoagulant **fgl2** prothombinase (Journal of Immunology (1998) 160 (545-549)).
AU Clark D.A.; Chaouat G.; Arck P.C.; Mittruecker H.W.; Levy G.A.
SO Journal of Immunology, (1 Mar 1999) 162/5 (3105).
ISSN: 0022-1767 CODEN: JOIMA3
ACCESSION NUMBER: 1999244538 EMBASE
TITLE: Erratum: Cutting edge: Cytokine-dependent abortion in CBA x DBA/2 mice is mediated by the procoagulant **fgl2** prothombinase (Journal of Immunology (1998) 160 (545-549)).
AUTHOR: Clark D.A.; Chaouat G.; Arck P.C.; Mittruecker H.W.; Levy G.A.
SOURCE: Journal of Immunology, (1 Mar 1999) 162/5 (3105).
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Errata
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English

L3 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2001 ACS
TI Cutting Edge: Cytokine-dependent abortion in CBA x DBA/2 mice is mediated by the procoagulant fg12 prothrombinase. [Erratum to document cited in CA128:139676]
AU Clark, David A.; Chaouat, Gerard; Arck, Petra C.; Mittruecker, Hans Willi; Levy, Gary A.
SO J. Immunol. (1999), 162(5), 3105
CODEN: JOIMA3; ISSN: 0022-1767
AB In the title and throughout the text, the word "prothombinase" should be "prothrombinase.".
ACCESSION NUMBER: 1999:221317 CAPLUS
DOCUMENT NUMBER: 130:222025
TITLE: Cutting Edge: Cytokine-dependent abortion in CBA x DBA/2 mice is mediated by the procoagulant fg12 prothrombinase. [Erratum to document cited in CA128:139676]
AUTHOR(S): Clark, David A.; Chaouat, Gerard; Arck, Petra C.; Mittruecker, Hans Willi; Levy, Gary A.
CORPORATE SOURCE: Dep. of Medicine, McMaster University, Hamilton, ON, L8N 3Z5, Can.
SOURCE: J. Immunol. (1999), 162(5), 3105
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

L3 ANSWER 13 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
TI Study of putative CIS-elements in MFGL2 promoter in response to nucleocapsid protein of murine hepatitis virus type 3.
AU Levy, Gary A. (1); Ning, Qin (1); Mc Lai, Michael; Marsden, Philip A.; Leibowitz, Julian; Phillips, M. James
SO Hepatology, (Oct., 1999) Vol. 30, No. 4 PART 2, pp. 502A.
Meeting Info.: 50th Annual Meeting and Postgraduate Courses of the

American Association for the Study of Liver Diseases Dallas, Texas, USA November 5-9, 1999 American Association for the Study of Liver Diseases . ISSN: 0270-9139.

ACCESSION NUMBER: 1999:509760 BIOSIS
DOCUMENT NUMBER: PREV199900509760
TITLE: Study of putative CIS-elements in MFGL2 promoter in response to nucleocapsid protein of murine hepatitis virus type 3.
AUTHOR(S): Levy, Gary A. (1); Ning, Qin (1); Mc Lai, Michael; Marsden, Philip A.; Leibowitz, Julian; Phillips, M. James
CORPORATE SOURCE: (1) Toronto Gen Hospital, Toronto, ON Canada
SOURCE: Hepatology, (Oct., 1999) Vol. 30, No. 4 PART 2, pp. 502A. Meeting Info.: 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 5-9, 1999 American Association for the Study of Liver Diseases . ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L3 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2001 ACS
TI A high-resolution radiation hybrid map of the proximal region of rat Chromosome 4
AU Al-Majali, Khulood M.; Glazier, Anne M.; Norsworthy, Penny J.; Wahid, Faisal N.; Cooper, Lisa D.; Wallace, Caroline A.; Scott, James; Lausen, Berthold; Aitman, Timothy J.
SO Mamm. Genome (1999), 10(5), 471-476
CODEN: MAMGEC; ISSN: 0938-8990
AB Radiation hybrid (RH) mapping has been used to produce genome maps in the human and mouse, but as yet the technique has been applied little to other species. We describe the use of RH mapping in the rat, using a newly available rat/hamster RH panel, to construct an RH map of the proximal part of rat Chromosome (Chr) 4. This region is of interest because quant. trait loci (QTLs) for defective insulin and catecholamine action, hypertension, and dyslipidemia map to this region. The RH map includes 23 rat genes or microsatellites previously mapped to this part of Chr 4, one rat gene not previously mapped in the rat, and markers for four new genes, homologs of which map to the syntenic region of the mouse genome. The RH map integrates genetic markers previously mapped on several rat crosses, increases the resoln. of existing maps, and may provide a suitable basis for phys. map construction and gene identification in this chromosomal region. Our results demonstrate the utility of RH mapping in the rat genome and show that RH mapping can be used to localize, in the rat genome, the homologs of genes from other species such as the mouse. This will facilitate identification of candidate genes underlying QTLs on this chromosomal segment.
ACCESSION NUMBER: 1999:427641 CAPLUS
DOCUMENT NUMBER: 131:318404
TITLE: A high-resolution radiation hybrid map of the proximal region of rat Chromosome 4

AUTHOR(S): Al-Majali, Khulood M.; Glazier, Anne M.; Norsworthy, Penny J.; Wahid, Faisal N.; Cooper, Lisa D.; Wallace, Caroline A.; Scott, James; Lausen, Berthold; Aitman, Timothy J.
CORPORATE SOURCE: MRC Clinical Sciences Centre, Molecular Medicine Group, Hammersmith Hospital, London, W12 ONN, UK
SOURCE: Mamm. Genome (1999), 10(5), 471-476
CODEN: MAMGEC; ISSN: 0938-8990
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 34
REFERENCE(S): (1) Abel, K; Genomics 1993, V17, P632 CAPLUS
(2) Ahlbom, B; Hum Genet 1997, P186 CAPLUS
(3) Aitman, T; Nat Genet 1997, V16, P197 CAPLUS
(4) Benham, F; Genomics 1989, V4, P509 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
TI The role of fibrinogen like protein (**fgl2**/fibroleukin) in xenograft rejection: Induction of **fgl2** prothrombinase by xenoserum.
AU Levy, Gary A. (1); Ding, Jinwen (1); Weiner, Daniel (1); Ning, Qin (1); Fung, Laisum (1); Marinov, Anton (1); Gorczynski, Reginald (1); Phillips, M. James (1); Zhong, Robert; Grant, David
SO Hepatology, (Oct., 1999) Vol. 30, No. 4 PART 2, pp. 188A.
Meeting Info.: 50th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA November 5-9, 1999 American Association for the Study of Liver Diseases
. ISSN: 0270-9139.
ACCESSION NUMBER: 1999:505735 BIOSIS
DOCUMENT NUMBER: PREV199900505735
TITLE: The role of fibrinogen like protein (**fgl2** /fibroleukin) in xenograft rejection: Induction of **fgl2** prothrombinase by xenoserum.
AUTHOR(S): Levy, Gary A. (1); Ding, Jinwen (1); Weiner, Daniel (1); Ning, Qin (1); Fung, Laisum (1); Marinov, Anton (1); Gorczynski, Reginald (1); Phillips, M. James (1); Zhong, Robert; Grant, David
CORPORATE SOURCE: (1) Toronto Gen Hospital, Toronto Canada
SOURCE: Hepatology, (Oct., 1999) Vol. 30, No. 4 PART 2, pp. 188A.
Meeting Info.: 50th Annual Meeting and Postgraduate Courses
of the American Association for the Study of Liver Diseases
Dallas, Texas, USA November 5-9, 1999 American Association for the Study of Liver Diseases
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L3 ANSWER 16 OF 29 MEDLINE DUPLICATE 5
TI The emerging role of immunoregulation of fibrinogen-related procoagulant **Fgl2** in the success or spontaneous abortion of early pregnancy in mice and humans.
AU Clark D A; Ding J W; Chaouat G; Coulam C B; August C; Levy G A
SO AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1999 Jul) 42 (1) 37-43.

Journal code: AEZ. ISSN: 1046-7408.

AB PROBLEM: Abortion of chromosomally normal embryos in the CBA X DBA/2 mating combination is triggered by release of Th1 cytokines (tumor necrosis factor [TNF]-alpha, interferon [IFN]-gamma, and interleukin [IL]-1), which cause abortion via a novel prothrombinase, **Fgl2**, and polymorphonuclear leukocytes. The site of activation may be maternal vascular endothelium on arteries and veins nourishing the placenta. Activation of coagulation is also prominent in spontaneous abortion of chromosomally normal human embryos. We asked where is **Fgl2** up-regulated in the uterus in murine abortions, and if similar **Fgl2** expression occurs in human pregnancy failure. METHODS: Control CBA X DBA/2 pregnant mice, or from mice injected with TNF-alpha + IFN-gamma on day 7.5 of gestation, were removed on day 8.5, fixed, sectioned, and subject to in situ hybridization for **Fgl2**. Sections were also stained for fibrin. Elective first trimester termination samples or biopsies taken early in the course of a recurrent miscarriage were similarly fixed, sectioned, and analyzed by in situ hybridization. Control and cytokine-treated mice were anticoagulated with heparin, an activator of antithrombin III, and/or the direct anti-thrombin inhibitor hirudin. RESULTS: Low level **Fgl2** expression localized to basal decidua remote from the embryo was noted in control mice; cytokine treatment, which causes greater than 80% of abortions, produced a striking up-regulation in this area as well as in a band at the junction of decidua and myometrium. Trophoblast also became strikingly positive. **Fgl2** expression was associated with increased fibrin staining. Anticoagulation significantly protected against abortions, but doses were limited by the complication of retroplacental hemorrhage. In tissue from normal first trimester pregnancy, minimal **Fgl2** positivity was seen in some villous syncytiotrophoblast, in villous stroma, cytotrophoblast, and in some cells in decidua. In spontaneous abortion of normal embryo, striking **Fgl2** positivity was seen in syncytiotrophoblast and extravillous cytotrophoblast, in association with areas of thrombus formation. CONCLUSIONS: **Fgl2** appears to be physiologically expressed and may protect against the internal danger of maternal and/or fetal bleeding during pregnancy and at parturition; a role in inhibiting transplacental traffic is also possible. External dangers in the form of stress, endotoxin, and antigens eliciting Th1 cytokine responses upregulate **Fgl2** prothrombinase in trophoblast as well as in decidua, which results in spontaneous abortion of immunogenetically "weaker" embryos.

ACCESSION NUMBER: 1999358396 MEDLINE
DOCUMENT NUMBER: 99358396
TITLE: The emerging role of immunoregulation of fibrinogen-related procoagulant **Fgl2** in the success or spontaneous abortion of early pregnancy in mice and humans.
AUTHOR: Clark D A; Ding J W; Chaouat G; Coulam C B; August C; Levy G A
CORPORATE SOURCE: Department of Medicine, McMaster University-Hamilton, Ontario, Canada.
SOURCE: AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1999 Jul) 42 (1) 37-43.
Journal code: AEZ. ISSN: 1046-7408.
PUB. COUNTRY: Denmark

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY WEEK: 19991203

L3 ANSWER 17 OF 29 MEDLINE DUPLICATE 6
TI Why did your mother reject you? Immunogenetic determinants of the response to environmental selective pressure expressed at the uterine level.
AU Clark D A; Arck P C; Chaouat G
SO AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1999 Jan) 41 (1) 5-22. Ref: 165
Journal code: AEZ. ISSN: 1046-7408.
AB PROBLEM: Maternal "rejection" of the implanted conceptus is considered to account for a significant proportion of miscarriages (abortions) in both humans and animals. Our understanding of mechanisms has been limited, and hence, explanations for nonrejection have remained largely speculative. Losses, when they occur, could represent either random accidental failure of protective mechanisms or a more purposeful discrimination. METHOD OF STUDY: An analysis of the most recent data. RESULTS AND CONCLUSIONS: The embryo is most akin to a parasite, and pregnancy is most akin to a host-parasite interaction. If one excludes chromosome abnormalities in the embryo as a cause of death, activation of coagulation mechanisms, leading to vasculitis affecting the maternal blood supply to the implanted embryo, appears to represent a major loss-causing mechanisms--a form of ischemic autoamputation. Proinflammatory T-helper (Th) 1-type cytokines trigger this process via upregulation of a novel prothrombinase, **fgl2**. Th2/3 cytokines, such as interleukin (IL)-4, IL-10, and transforming growth factor (TGF)-beta 2, may antagonize the processes involved. Cytokine balance is determined by the genetics of the mother, which regulate her response to stress; endotoxin (LPS); and paternal antigens, selectively expressed on the trophoblast of the embryo, via imprinting. Based on studies in abortion-prone mice, where immunity to paternal alloantigens prevents loss, three distinct gene products in the embryo are proposed to determine the cytokine response to maternal lymphomyeloid cells in the uterus.
ACCESSION NUMBER: 1999197856 MEDLINE
DOCUMENT NUMBER: 99197856
TITLE: Why did your mother reject you? Immunogenetic determinants of the response to environmental selective pressure expressed at the uterine level.
AUTHOR: Clark D A; Arck P C; Chaouat G
CORPORATE SOURCE: McMaster University, Hamilton, Ontario, Canada.
SOURCE: AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1999 Jan) 41 (1) 5-22. Ref: 165
Journal code: AEZ. ISSN: 1046-7408.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909

ENTRY WEEK: 19990902

L3 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2001 ACS
TI Protein **Fgl2** inhibitors for modulation of immune coagulation
IN Levy, Gary
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
AB Methods for mediating immune coagulation using novel antibodies and compds. are described. A protein **Fgl2** having direct prothrombinase activity has been identified. Inhibitors of **Fgl2** such as monoclonal antibodies are useful in preventing and treating diseases which require a redn. in immune coagulation including bacterial and viral infections, allograft and xenograft rejection, glomerulonephritis, cancer, a no. of gastrointestinal diseases and fetal loss.

ACCESSION NUMBER: 1998:761808 CAPLUS
DOCUMENT NUMBER: 130:24098
TITLE: Protein **Fgl2** inhibitors for modulation of immune coagulation
INVENTOR(S): Levy, Gary
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851335	A1	19981119	WO 1998-CA475	19980515
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874213	A1	19981208	AU 1998-74213	19980515
EP 975361	A1	20000202	EP 1998-921301	19980515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-46537 19970515
US 1997-61684 19971010
WO 1998-CA475 19980515

REFERENCE COUNT: 9
REFERENCE(S):
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(2) Genentech Inc; EP 0278776 A 1988 CAPLUS
(3) Koyama, T; Proc Natl Acad Sci USA 1987, V84, P1609 CAPLUS
(4) Parr, R; 5033, Journal of Virology 1995, V69(8) CAPLUS
(5) Pope, M; The Journal of Immunology 1996, V156, P3342 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2001 ACS
TI Murine hepatitis virus strain 3 induces the macrophage prothrombinase fgl-2 through p38 mitogen-activated protein kinase activation
AU McGilvray, Ian D.; Lu, Ziu; Wei, Alice C.; Dackiw, Alan P. B.; Marshall, John C.; Kapus, Andras; Levy, Gary; Rotstein, Ori D.
SO J. Biol. Chem. (1998), 273(48), 32222-32229
CODEN: JBCHA3; ISSN: 0021-9258
AB The clin. syndrome of acute liver failure produced by fulminant viral hepatitis can be reproduced in mice by infection with murine hepatitis virus strain 3 (MHV-3). Although it is clear that MHV-3-induced hepatitis depends upon macrophage activation and the expression of a specific prothrombinase, fgl-2, the signaling pathways involved in virally stimulated cell activation are unclear. Since we had previously found that MHV-3 induces the tyrosine phosphorylation of cellular proteins, we investigated the roles of the mitogen-activated protein kinase (MAPK) proteins. In a series of Western blots, immunopptn. and in vitro kinase assay studies, we found that both the extracellular signal-related kinase (ERK) and p38 MAPK proteins are tyrosine-phosphorylated and activated following exposure of murine peritoneal exudative macrophages (PEM) to MHV-3. Although p38 phosphorylation and activity are induced soon after MHV-3 exposure, peaking by 1-5 min, ERK phosphorylation and activity increase more gradually, peaking at 20-30 min and gradually fading thereafter. Interestingly, whereas selective p38 inhibition with SB203580 (1-20 .mu.M) abolished the virally stimulated induction of fgl-2 mRNA, protein, and functional activity, selective ERK inhibition with PD98059 (1-50 .mu.M) limited fgl-2 functional activity but had little to no effect on fgl-2 mRNA or protein levels. Moreover, whereas inhibition of ERK had no effect on p38 activity, p38 inhibition consistently increased MHV-3-induced ERK activity. To ensure that these pathways were relevant in vivo, MHV-3 was injected i.p., and peritoneal exudative macrophages were collected. Again, MHV-3 exposure led to increased p38 and ERK tyrosine phosphorylation. These data argue that MHV-3 induces tightly interconnected ERK and p38 MAPK cascades in the macrophage both in vitro and in vivo. Although the ERK and p38 MAPK proteins have discordant effects at the level of fgl-2 expression, both converge at the level of its activity, suggesting that targeted MAPK inhibition may ultimately be useful in the modulation of viral hepatitis.
ACCESSION NUMBER: 1998:783684 CAPLUS
DOCUMENT NUMBER: 130:138251
TITLE: Murine hepatitis virus strain 3 induces the macrophage prothrombinase fgl-2 through p38 mitogen-activated protein kinase activation
AUTHOR(S): McGilvray, Ian D.; Lu, Ziu; Wei, Alice C.; Dackiw, Alan P. B.; Marshall, John C.; Kapus, Andras; Levy, Gary; Rotstein, Ori D.
CORPORATE SOURCE: Departments of Surgery and Medicine, Toronto Hospital, General Division and the University of Toronto, Toronto, M5G 2C4, Can.
SOURCE: J. Biol. Chem. (1998), 273(48), 32222-32229
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 71
REFERENCE(S): (3) Beauchemin, N; Oncogene 1997, V14, P783 CAPLUS
(4) Benn, J; J Virol 1996, V70, P4978 CAPLUS
(5) Benn, J; Proc Natl Acad Sci U S A 1994, V91, P10350 CAPLUS
(6) Benn, J; Proc Natl Acad Sci U S A 1995, V92, P11215 CAPLUS
(7) Bouchard, B; J Biol Chem 1997, V272, P9244 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 29 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Erratum: Fulminant hepatic failure in murine hepatitis virus strain 3 infection: Tissue-specific expression of a novel **fgl2** prothrombinase (Journal of Virology 71:12 (9225-9229)).
AU Ding J.W.; Ning Q.; Liu M.F.; Lai A.; Leibowitz J.; Peltekian K.M.; Cole E.H.; Fung L.S.; Holloway C.; Marsden P.A.; Yeger H.; Phillips M.J.; Levy G.A.
SO Journal of Virology, (1998) 72/4 (3504).
ISSN: 0022-538X CODEN: JOVIAM
ACCESSION NUMBER: 1998127413 EMBASE
TITLE: Erratum: Fulminant hepatic failure in murine hepatitis virus strain 3 infection: Tissue-specific expression of a novel **fgl2** prothrombinase (Journal of Virology 71:12 (9225-9229)).
AUTHOR: Ding J.W.; Ning Q.; Liu M.F.; Lai A.; Leibowitz J.; Peltekian K.M.; Cole E.H.; Fung L.S.; Holloway C.; Marsden P.A.; Yeger H.; Phillips M.J.; Levy G.A.
CORPORATE SOURCE: J.W. Ding, Multi-Organ Transplant Program, Department of Medicine, Toronto Hospital, Toronto, Ont., Canada
SOURCE: Journal of Virology, (1998) 72/4 (3504).
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Errata
FILE SEGMENT: 004 Microbiology
LANGUAGE: English

L3 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2001 ACS
TI Fulminant hepatic failure in murine hepatitis virus strain 3 infection: tissue-specific expression of a novel **fgl2** prothrombinase. [Erratum to document cited in CA128:33126]
AU Ding, J. W.; Ning, Q.; Liu, M. F.; Lai, A.; Leibowitz, J.; Peltekian, K. M.; Cole, E. H.; Fung, L. S.; Holloway, C.; Marsden, P. A.; Yeger, H.; Phillips, M. James; Levy, Gary A.
SO J. Virol. (1998), 72(4), 3504
CODEN: JOVIAM; ISSN: 0022-538X
AB Vol. 71, no. 12, p. 9225 and 9229: Figures 1 and 7 were transposed; the legends are correct.
ACCESSION NUMBER: 1998:205185 CAPLUS
DOCUMENT NUMBER: 128:203706
TITLE: Fulminant hepatic failure in murine hepatitis virus strain 3 infection: tissue-specific expression of a novel **fgl2** prothrombinase. [Erratum to document cited in CA128:33126]
AUTHOR(S): Ding, J. W.; Ning, Q.; Liu, M. F.; Lai, A.; Leibowitz,
J.; Peltekian, K. M.; Cole, E. H.; Fung, L. S.;

	Holloway, C.; Marsden, P. A.; Yeger, H.; Phillips, M. James; Levy, Gary A.
CORPORATE SOURCE:	Multi-Organ Transplant Program, Departments of Medicine and Pathology, Toronto Hospital, University Toronto, Toronto, ON, Can.
SOURCE:	J. Virol. (1998), 72(4), 3504 CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER:	American Society for Microbiology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

L3 ANSWER 22 OF 29 MEDLINE DUPLICATE 7

TI Ribavirin inhibits viral-induced macrophage production of TNF, IL-1, the procoagulant **fgl2** prothrombinase and preserves Th1 cytokine production but inhibits Th2 cytokine response.

AU Ning Q; Brown D; Parodo J; Cattral M; Gorczynski R; Cole E; Fung L; Ding J W; Liu M F; Rotstein O; Phillips M J; Levy G

SO JOURNAL OF IMMUNOLOGY, (1998 Apr 1) 160 (7) 3487-93.
Journal code: IFB. ISSN: 0022-1767.

AB Ribavirin, a synthetic guanosine analogue, possesses a broad spectrum of activity against DNA and RNA viruses. It has been previously shown to attenuate the course of fulminant hepatitis in mice produced by murine hepatitis virus strain 3. We therefore studied the effects of ribavirin on murine hepatitis virus strain 3 replication, macrophage production of proinflammatory mediators including TNF, IL-1, and the procoagulant activity (PCA), **fgl2** prothrombinase; and Th1/Th2 cytokine production. Although ribavirin had inhibitory effects on viral replication (<1 log), even at high concentrations complete eradication of the virus was not seen. In contrast, at physiologic concentrations (up to 500 microg/ml), ribavirin markedly reduced viral-induced parameters of macrophage activation. With ribavirin treatment, the concentrations of PCA, TNF-alpha and IL-1beta all decreased to basal concentrations: PCA from 941 +/- 80 to 34 +/- 11 mU/10(6) cells; TNF-alpha from 10.73 +/- 2.15 to 2.74 +/- 0.93 ng/ml; and IL-1beta from 155.91 +/- 22.62 to 5.74 +/- 0.70 pg/ml. The inhibitory effects of ribavirin were at the level of gene transcription as evidenced by Northern analysis. Both in vitro and in vivo, ribavirin inhibited the production of IL-4 by Th2 cells, whereas it did not diminish the production of IFN-gamma in Th1 cells. In contrast, ribavirin had no inhibitory effect on TNF-alpha and IL-1beta production in LPS-stimulated macrophages. These results suggest that the beneficial effects of ribavirin are mediated by inhibition of induction of macrophage proinflammatory cytokines and Th2 cytokines while preserving Th1 cytokines.

ACCESSION NUMBER:	1998189797 MEDLINE
DOCUMENT NUMBER:	98189797
TITLE:	Ribavirin inhibits viral-induced macrophage production of TNF, IL-1, the procoagulant **fgl2** prothrombinase and preserves Th1 cytokine production but inhibits Th2 cytokine response.
AUTHOR:	Ning Q; Brown D; Parodo J; Cattral M; Gorczynski R; Cole E; Fung L; Ding J W; Liu M F; Rotstein O; Phillips M J; Levy G

CORPORATE SOURCE: Multiogran Transplant Program, Department of Medicine, Toronto Hospital, University of Toronto, Ontario, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Apr 1) 160 (7) 3487-93. Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199806
ENTRY WEEK: 19980604

L3 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2001 ACS
TI The pattern of induction of apoptosis during infection with MHV-3 correlates with strain variation in resistance and susceptibility to lethal hepatitis
AU Belyavskyi, Michail; Levy, Gary A.; Leibowitz, Julian L.
SO Adv. Exp. Med. Biol. (1998), 440(Coronaviruses and Arteriviruses), 619-625
CODEN: AEMBAP; ISSN: 0065-2598
AB In the present study, the possibility that strain specific differences in the induction of apoptosis in macrophages could play a role in the resistance of strain A/J mice to MHV-3-induced hepatitis was investigated.
MHV-3-infected macrophages from Balb/c and A/J mice were analyzed at various time points after infection. Apoptosis in A/J macrophages could be detected at 8 h post infection and increased by 12 h, when almost 50-70% of the infected cells were undergoing apoptosis. In Balb/c macrophages, apoptotic changes were less pronounced and were obsd. in only 5-10% of the cells. MHV-3 induced apoptosis was inversely correlated with the ability of this virus to induce expression of fgl-2 prothrombinase protein and syncytia formation. Infected macrophages, from A/J mice did not express fgl-2 protein and did not form syncytia. In contrast, infection of Balb/c derived macrophages resulted in fgl-2 expression and extensive syncytia formation. These data fit a model in which apoptosis of virally infected cells is a protective response which eliminates cells whose survival might be harmful for the whole organism.
ACCESSION NUMBER: 1998:696456 CAPLUS
DOCUMENT NUMBER: 130:92712
TITLE: The pattern of induction of apoptosis during infection with MHV-3 correlates with strain variation in resistance and susceptibility to lethal hepatitis
AUTHOR(S): Belyavskyi, Michail; Levy, Gary A.; Leibowitz, Julian L.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Texas AandM University College of Medicine, College Station, TX, 77843-1114, USA
SOURCE: Adv. Exp. Med. Biol. (1998), 440(Coronaviruses and Arteriviruses), 619-625
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English

REFERENCE COUNT: 11
REFERENCE(S):
(1) Belyavskyi, M; Virology 1994, V204, P132 CAPLUS
(2) Cuff, S; Immun Cell Biol 1996, V74, P527 CAPLUS
(3) Dindzans, V; J Immunol 1985, V135, P4189 CAPLUS
(8) Parr, R; J Virol 1995, V69, P5033 CAPLUS
(10) Schutte, B; Cytometry 1987, V8, P372 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 29 MEDLINE DUPLICATE 8
TI Expression of the **fgl2** and its protein product (prothrombinase) in tissues during murine hepatitis virus strain-3 (MHV-3) infection.
AU Ding J W; Ning Q; Liu M F; Lai A; Peltekian K; Fung L; Holloway C; Yeger H; Phillips M J; Levy G A
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 440 609-18. Journal code: 2LU. ISSN: 0065-2598.
AB Murine Hepatitis Virus Strain 3 (MHV-3) produces fulminant hepatitis with 80-90% mortality in Balb/cJ mice. Previous studies in our laboratory have shown that peritoneal macrophages from MHV-3 infected mice produce a procoagulant (PCA) which has the ability to cleave prothrombin to thrombin (prothrombinase) encoded by the gene **fgl2** located on chromosome 5. PCA accounts for sinusoidal thrombosis and hepatic necrosis and the necrosis and mortality can be prevented by treatment of animals with a monoclonal antibody to PCA. These present studies were designed to examine the expression of this gene (mRNA by Northern analysis and in situ hybridization) and the gene product PCA (immunochemistry) in tissues recovered from MHV-3 infected Balb/cJ mice in an attempt to explain the liver specific nature of MHV-3 disease. **Fgl2** gene expression was detected as early as 8 hours after MHV-3 infection which persisted to 48 hours in the liver, spleen and lungs whereas no gene expression was seen in the brain or kidneys despite the fact that equivalent viral titers were detected in all tissues at all times. In the liver, **fgl2** gene expression was confined to endothelial and Kupffer cells with no expression in hepatocytes. Immunochemistry localized the PCA protein to Kupffer cells and endothelial cells and necrotic foci within the liver. No PCA protein was detected by immunochemistry in any other tissues at any time during the course of MHV-3 infection. These results explain the liver specific nature (fulminant hepatitis) of MHV-3 infection and provides further evidence for the role of PCA in the pathogenesis of fulminant hepatitis. MHV-3 induces selective transcription of the gene **fgl2** and only hepatic reticuloendothelial cells produce functional protein (PCA) which is known to account for fulminant hepatic failure produced by MHV-3.
ACCESSION NUMBER: 1998455656 MEDLINE
DOCUMENT NUMBER: 98455656
TITLE: Expression of the **fgl2** and its protein product (prothrombinase) in tissues during murine hepatitis virus strain-3 (MHV-3) infection.
AUTHOR: Ding J W; Ning Q; Liu M F; Lai A; Peltekian K; Fung L; Holloway C; Yeger H; Phillips M J; Levy G A
CORPORATE SOURCE: Department of Multi Organ Transplantation Program and Medicine, Toronto Hospital, Ontario, Canada.
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 440 609-18.

Journal code: 2LU. ISSN: 0065-2598.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY WEEK: 19990303

L3 ANSWER 25 OF 29 MEDLINE DUPLICATE 9
TI Cytokine-dependent abortion in CBA x DBA/2 mice is mediated by the procoagulant **fgl2** prothrombinase [correction of prothombinase] [published erratum appears in J Immunol 1999 Mar 1;162(5):3105].
AU Clark D A; Chaouat G; Arck P C; Mittruecker H W; Levy G A
SO JOURNAL OF IMMUNOLOGY, (1998 Jan 15) 160 (2) 545-9.
Journal code: IFB. ISSN: 0022-1767.
AB Spontaneous resorption in the CBA x DBA/2 model is attributed to NK cells, macrophages, and Th1-type cytokines. In vivo depletion of NK cells by anti-asialoGM1 Ab or macrophage depletion by silicon dioxide treatment reduced abortion rates, which could no longer be boosted by injecting TNF-alpha (which activates NK cells) or IFN-gamma (which activates macrophages). TNF-alpha + gamma-IFN coadministration aborted >80% of the embryos whether or not NK cells or macrophages had been depleted or estradiol + progesterone was injected to correct potential reduction in ovarian function by cytokines. The cytokines also aborted IRF1+/+ C57BL/6 but not IRF1-/- females pregnant by IRF1+/+ DBA/2. Both spontaneous and cytokine-boosted abortions in CBA x DBA/2 were blocked by Ab to **fgl2** prothrombinase [corrected] expressed by cytokine-stimulated vascular endothelial cells and monocytes; in vivo Ab depletion of granulocytes also prevented TNF-alpha + IFN-gamma-induced abortions. Cytokine-triggered thrombotic/inflammatory processes in maternal uteroplacental blood vessels causes abortion.
ACCESSION NUMBER: 1998211610 MEDLINE
DOCUMENT NUMBER: 98211610
TITLE: Cytokine-dependent abortion in CBA x DBA/2 mice is mediated by the procoagulant **fgl2** prothrombinase [correction of prothombinase] [published erratum appears in J Immunol 1999 Mar 1;162(5):3105].
AUTHOR: Clark D A; Chaouat G; Arck P C; Mittruecker H W; Levy G A
CORPORATE SOURCE: McMaster University, Hamilton, Ontario, Canada.. clarkd@fhs.csu.McMaster.ca
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Jan 15) 160 (2) 545-9.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199807

L3 ANSWER 26 OF 29 BIOSIS COPYRIGHT 2001 BIOSIS
TI Cloning and characterization of the human prothrombinase gene (H-**fgl2**) and its role in human hepatitis.
AU Ding, J. W. (1); Liu, M. F. (1); Yuwaraj, S. (1); Leibowitz, J.; Marsden, P. (1); Ning, Q. (1); Kovalinka, A. (1); Phillips, M. J. (1); Levy, G. A. (1)

SO Hepatology, (Oct., 1998) Vol. 28, No. 4 PART 2, pp. 254A.
Meeting Info.: Biennial Scientific Meeting of the International Association for the Study of the Liver and the 49th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Chicago, Illinois, USA November 4-10, 1998 International Association for the Study of the Liver
. ISSN: 0270-9139.

ACCESSION NUMBER: 1998:525321 BIOSIS
DOCUMENT NUMBER: PREV199800525321
TITLE: Cloning and characterization of the human prothrombinase gene (H-**fgl2**) and its role in human hepatitis.
AUTHOR(S): Ding, J. W. (1); Liu, M. F. (1); Yuwaraj, S. (1); Leibowitz, J.; Marsden, P. (1); Ning, Q. (1); Kovalinka, A.
(1); Phillips, M. J. (1); Levy, G. A. (1)
CORPORATE SOURCE: (1) Multi Organ Transplant Program, University Toronto-Toronto Hospital, Toronto, ON Canada
SOURCE: Hepatology, (Oct., 1998) Vol. 28, No. 4 PART 2, pp. 254A.
Meeting Info.: Biennial Scientific Meeting of the International Association for the Study of the Liver and the 49th Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Chicago, Illinois, USA November 4-10, 1998 International Association for the Study of the Liver
. ISSN: 0270-9139.
DOCUMENT TYPE: Conference
LANGUAGE: English

L3 ANSWER 27 OF 29 MEDLINE DUPLICATE 10
TI Coronavirus MHV-3-induced apoptosis in macrophages.
AU Belyavsky M; Belyavskaya E; Levy G A; Leibowitz J L
SO VIROLOGY, (1998 Oct 10) 250 (1) 41-9.
Journal code: XEA. ISSN: 0042-6822.
AB Infection with mouse hepatitis virus strain 3 (MHV-3) results in lethal fulminant hepatic necrosis in fully susceptible BALB/c mice compared to the minimal disease observed in resistant strain A/J mice. Macrophages play a central role in the pathogenesis of MHV-3-induced hepatitis. In the
present study we have shown that MHV-3 infection of macrophages induces these cells to undergo apoptosis. Three methods to detect apoptosis were applied: flow cytometry analysis of nuclear DNA content, fluorescence microscopic visualization of apoptotic cells labeled by the TUNEL assay, and gel electrophoresis to detect DNA laddering. Apoptosis in A/J and BALB/c macrophages was first detected at 8 h postinfection (p.i.) and reached a maximum by 12 h p.i. The degree of MHV-3-induced apoptosis was much greater in A/J-derived macrophages than in BALB/c-derived cells. Apoptosis was inversely correlated with the development of typical MHV cytopathology, namely syncytia formation. Infected macrophages from A/J mice did not form synctia in contrast to the extensive synctia formation observed in BALB/c-derived macrophages. In MHV-3-infected BALB/c macrophage cultures, apoptotic cells were not incorporated into syncytia. Apoptosis was also inversely correlated with the expression of MHV-3-induced **fgl2** prothrombinase in macrophages. These results add the murine coronavirus MHV-3 to the list of RNA-containing viruses capable of inducing apoptosis. Copyright 1998 Academic Press.
ACCESSION NUMBER: 1998445444 MEDLINE
DOCUMENT NUMBER: 98445444
TITLE: Coronavirus MHV-3-induced apoptosis in macrophages.

AUTHOR: Belyavsky M; Belyavskaya E; Levy G A; Leibowitz J L
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Texas A&M University College of Medicine, 208 Reynolds Building, College Station, Texas, 77843-1114, USA.
CONTRACT NUMBER: PPG11810
SOURCE: VIROLOGY, (1998 Oct 10) 250 (1) 41-9.
Journal code: XEA. ISSN: 0042-6822.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199901
ENTRY WEEK: 19990104

L3 ANSWER 28 OF 29 MEDLINE DUPLICATE 11
TI Fulminant hepatic failure in murine hepatitis virus strain 3 infection: tissue-specific expression of a novel **fgl2** prothrombinase [published erratum appears in J Virol 1998 Apr;72(4):3504].
AU Ding J W; Ning Q; Liu M F; Lai A; Leibowitz J; Peltekian K M; Cole E H; Fung L S; Holloway C; Marsden P A; Yeger H; Phillips M J; Levy G A
SO JOURNAL OF VIROLOGY, (1997 Dec) 71 (12) 9223-30.
Journal code: KCV. ISSN: 0022-538X.
AB Activation of the immune coagulation system has been implicated in the pathogenesis of fulminant liver failure caused by murine hepatitis virus strain 3 (MHV-3). The recent discovery of the **fgl2** gene, which encodes for MHV-3-induced prothrombinase (**fgl2** prothrombinase), allows for fundamental studies to determine the molecular basis for fulminant liver failure. Transcription of the **fgl2** gene and translation of the protein it encodes were examined in the liver and other organs of susceptible mice following MHV-3 infection. No constitutive expression of the **fgl2** gene or the **fgl2** prothrombinase was detected. Within 12 to 24 h of MHV-3 infection, however, **fgl2** gene transcripts were detected in large amounts in the liver, spleen, and lungs, all of which are rich in reticuloendothelial cells, but were only focally present in small amounts in the kidney and brain. There was sequential detection of **fgl2** prothrombinase in the liver, where it was localized specifically to the endothelium of intrahepatic veins and hepatic sinusoids; this was allowed by fibrin deposition, which resulted in confluent hepatocellular necrosis. These results provide further evidence for the role of the selective expression of this novel **fgl2** prothrombinase in the pathogenesis of MHV-3-induced fulminant liver failure.
ACCESSION NUMBER: 1998037632 MEDLINE
DOCUMENT NUMBER: 98037632
TITLE: Fulminant hepatic failure in murine hepatitis virus strain 3 infection: tissue-specific expression of a novel **fgl2** prothrombinase [published erratum appears in J Virol 1998 Apr;72(4):3504].
AUTHOR: Ding J W; Ning Q; Liu M F; Lai A; Leibowitz J; Peltekian K M; Cole E H; Fung L S; Holloway C; Marsden P A; Yeger H; Phillips M J; Levy G A
CORPORATE SOURCE: Multi-Organ Transplant Program and Department of Medicine, Toronto Hospital, Ontario, Canada.
SOURCE: JOURNAL OF VIROLOGY, (1997 Dec) 71 (12) 9223-30.
Journal code: KCV. ISSN: 0022-538X.
PUB. COUNTRY: United States

	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Cancer Journals; Priority Journals
ENTRY MONTH:	199803

L3 ANSWER 29 OF 29 MEDLINE DUPLICATE 12
TI Mouse hepatitis virus-3 induced prothrombinase (**Fgl2**) maps to proximal chromosome 5.
AU Qureshi S T; Clermont S; Leibowitz J; Fung L S; Levy G; Malo D
SO GENOMICS, (1995 Sep 1) 29 (1) 307-9.
Journal code: GEN. ISSN: 0888-7543.

ACCESSION NUMBER:	96079133 MEDLINE
DOCUMENT NUMBER:	96079133
TITLE:	Mouse hepatitis virus-3 induced prothrombinase (**Fgl2**) maps to proximal chromosome 5.
AUTHOR:	Qureshi S T; Clermont S; Leibowitz J; Fung L S; Levy G; Malo D
CORPORATE SOURCE:	Department of Medicine, McGill University, Montreal, Quebec, Canada.
SOURCE:	GENOMICS, (1995 Sep 1) 29 (1) 307-9. Journal code: GEN. ISSN: 0888-7543.
PUB. COUNTRY:	United States
	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199604

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